

REMARKS

Reconsideration of this patent application is respectfully requested in view of the foregoing amendments, and the following remarks. Claims 1-9 are in the application. Claims 2 and 6 have been amended. Claims 10-16 have been added. No new matter has been added.

The Examiner rejected claims 1 and 4-9 under 35 USC 103 as being unpatentable over Mulqueen et al. and Krich et al. The Examiner stated that claims 2 and 3 would be patentable if rewritten in independent form. Applicant has amended claim 2 to place it in independent form, and has added new claims 10-16, to depend therefrom. Claims 10-16 correspond to original claims 3-9, which depend from claim 1.

Regarding the rejection of claims 1 and 4-9, Applicant respectfully traverses. Claim 1 relates to a process comprising " . . . adding a base to a reaction mixture comprising a compound of the general formula (1) . . . and an electrophile E-Y. Mulqueen et al. teaches a process where the thiazolidine gets deprotonated using a base in a first step "... at - 90°C, and then iodomethane [the electrophile] was added . . ." in a subsequent and separate

step (cf. Mulqueen: Experimental, Preparation of compound 10, p. 5363; Kirch: Example 2, 3rd step).

Comparison experiments showed, that using the process of Mulqueen et al. by adding the electrophile in a subsequent step at a temperature of greater than - 40°C, none of the desired product can be obtained (but decomposition products only). However, using low temperatures of -90°C in a technical scale is extremely difficult and expensive. Furthermore, the reaction time is extremely long.

The problem to solve in Mulqueen and Kirch was to provide a process which leads to high yields using economic and technically realizable reaction conditions. The problem was solved in using another reaction sequence, as described in Kirch. The new sequence allows the use of higher temperatures and nevertheless leads to high yields. The difference between the teaching of Mulqueen et al. and Kirch et al. is not the application of an increased temperature, the difference is an alternative reaction sequence which allows the use of an increased temperature.

The results of the present invention are surprising, because the reaction sequence taught by Mulqueen et al. carried out at

higher temperatures only leads to decomposition of the reactants. From a chemical point of view the result is surprising because this enantioselective reaction passes a planar transition state (intermediate, cf. compound 9 in Mulqueen et al.). A person skilled in the art would expect that at higher temperatures, both enantiomers will be obtained, because the activation energy for both possible substitutions (frontside/backside) is available, resulting in lower enantioselectivity or even a racemic product.

Additionally, Mulqueen et al. report with reference to Seebach et al. that certain intermediates undergo  $\beta$ -elimination (page 5361, Scheme 2).

Therefore, it is surprising to a person skilled in the art that (i) the labile intermediate reacts even at higher temperatures in a controlled manner (no  $\beta$ -elimination, no decomposition) and (ii) even only one enantiomer is obtained (although both enantiomers could result due to increased activation energy). There is no hint for the person skilled in the art in the teaching of Mulqueen et al. that this surprising result can be obtained by changing the reaction sequence (adding the base to a mixture comprising the thiazoldine and the electrophile) as claimed in claim 1 of the present invention. In

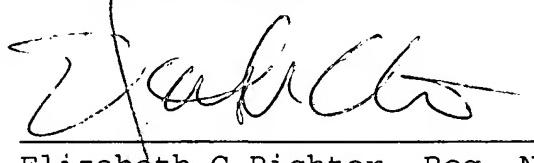
fact, the teaching of Mulqueen et al. would lead a person skilled in the art to use other reaction conditions due to an expected side reaction

The teaching of Kirch et al. is directed to another reaction sequence: The methylation is carried out using a racemic starting material and resulting in a racemic product. The racemic product is then separated into its enantiomers by a subsequent proceeding. The teaching of Kirch et al. is not directed to an enantioselective methylation as claimed in claim 1. Furthermore the "slightly different in structure" (cf. office action, page 4) will certainly lead to another chemical behaviour with respect to decomposition and  $\beta$ -elimination. Therefore the teaching of Kirch et al. is irrelevant for the claimed invention.

Thus, combining Kirch with Mulqueen would not lead to the present invention, because neither reference teaches or suggests the specific chemical composition and conditions claimed in claim 1 of the present invention. Such a composition and conditions, as described above, were completely unexpected based on the teachings of Mulqueen and Kirch. Accordingly, Applicant submits that claims 1 and 4-9 are patentable over the cited references,

taken either singly or in combination. Early allowance of the original and new claims is respectfully requested.

Respectfully submitted,  
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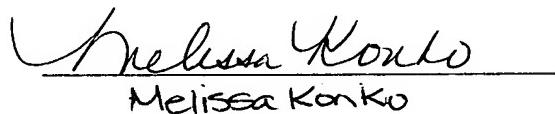
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